UNIVERSITÀ DI TRENTO
Dipartimento di
Biologia Cellulare, Computazionale e Integrata - CIBIO

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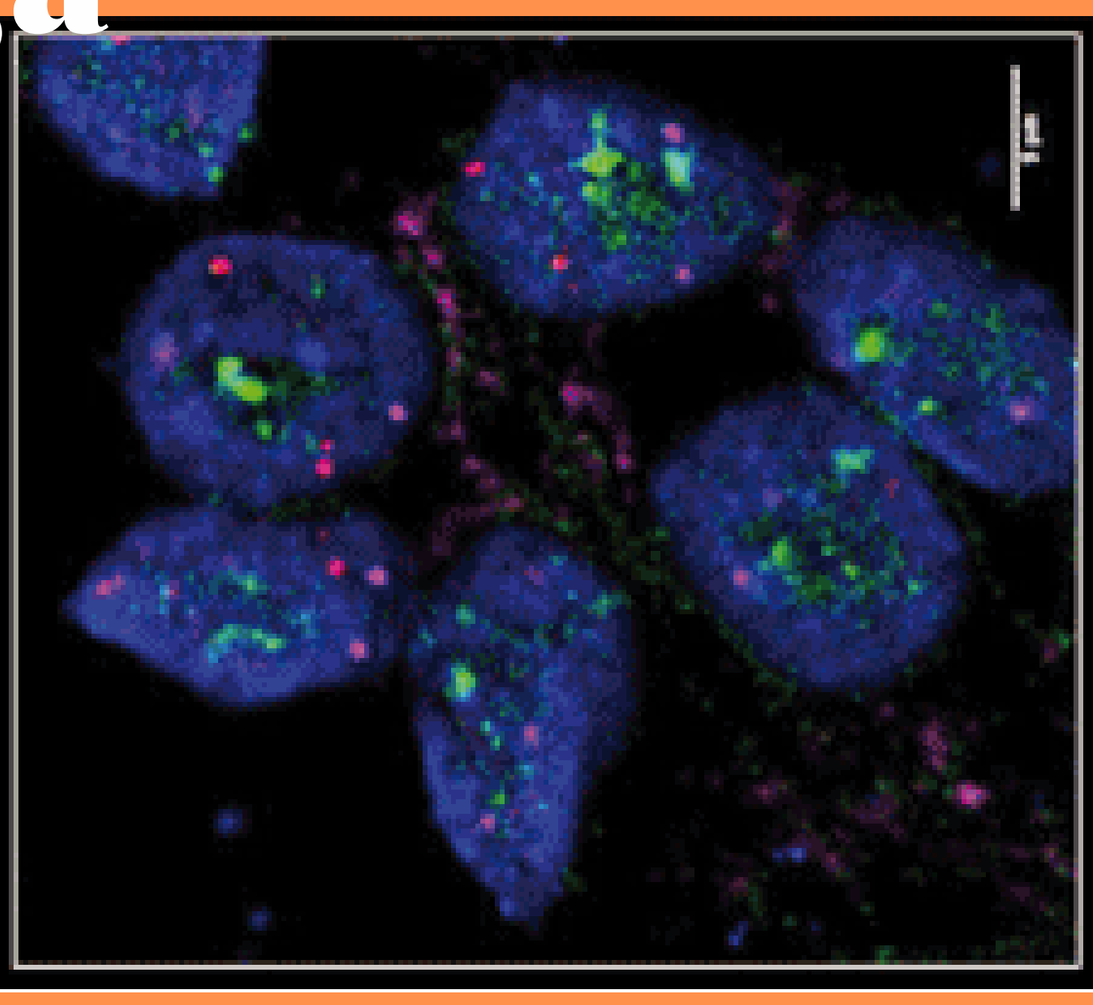
21.09 at 2 p.m. | room A108 Povo1

LINE1 REGULATE HUMAN T CELL FUNCTION BY ASSEMBLING CHROMATIN INTO CONDENSATES

Beatrice Bodega

ISTITUTO NAZIONALE DI GENETICA MOLECOLARE - INGM "ROMEO ED ENRICA INVERNIZZI"

DIPARTIMENTO DI BIOSCIENZE, UNIVERSITÀ DEGLI STUDI DI MILANO



EPIGENETIC SEMINAR

We have recently uncovered a novel mechanism of gene expression control that regulate the switch from T cell quiescence to activation and exhaustion that involves the splicing of long interspersed nuclear element 1 (LINE1) as exons of novel transcript variants (hereafter called LINE1-transcripts). We discovered that LINE1-transcripts act in complex with Nucleolin/KAP1 to keep paused the expression of the corresponding T-cell activation genes, sustaining T cell quiescence and exhaustion. Notably, LINE1-transcript depletion reverts T cell exhaustion increasing anti-tumoral immune response (Marasca F. et al, Nature Genetics, 2022). This LINE1-transcript/KAP1/Nucleolin complex occupies large domains to naïve CD4+ T-cells quiescence. We are addressing the function of this complex at chromatin exploiting a multi-omics strategy based on ChIP-seq for KAP1, Nucleolin, and several histone marks, RADICL-seq to map LINE1-transcripts location in the genome and Hi-C. Besides, we are now testing the hypothesis that LINE1-transcripts exert a novel epigenetic function to maintain T lymphocyte quiescence or exhaustion through the assembly of phase-separated chromatin bodies, we observe that LINE1-transcript concentration dictate KAP1 condensate assembly, abundance, and functionality, ultimately regulating the quiescent state at epigenetic level.
Overall, we are introducing the concept that LINE1 generate a new class of noncoding RNAs is that control T cell function and represents a novel regulatory checkpoint to be targeted for untapped therapeutic approaches.

HOSTED BY FULVIO CHIACCHIERA

DEPARTMENT OF CELLULAR, COMPUTATIONAL AND INTEGRATIVE BIOLOGY - CIBIO
VIA SOMMARIVE, 9 | 38123 - POVO (TN)
COMUNICAZIONE.CIBIO@UNITN.IT